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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/297,040	07/21/1999	PETER MOSE LARSEN	2012.0390004	9201

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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/297,040	MOSE LARSEN ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7 April 2003 (Paper No. 23)* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-5,9,12-18,20,21 and 24-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8,10,11,19, 22 and 23* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *25* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' requests for extension of time for 1 month filed 21 July 21 1999 (Paper No. 3), 5 months filed 4 April 2001 (Paper No. 7), 2 months filed 12 September 2001 (Paper No. 11), 5 months filed 19 September 2002 (Paper No. 18, and 4 months filed 7 April 2003 (Paper No. 22) have been entered. IDS submitted 8 May 2001 (Paper No. 9) is acknowledged.

Election/Restrictions

The current Applicant's election of claims 6-11, 19 and 22-23 of Group II with traverse filed 7 April 2003 (Paper No. 23) is acknowledged. The traversal is on the ground(s) that the claims of Group II are related to claims 1-5, 14-15 and 12-13 because all of these claims have a common technical feature as being directed to diabetes-mediating proteins (see page 2, the second paragraph); thus, applicants assert that the claims 1-11, 12-15, 19 and 22-23 should be examined together. The applicants' argument is unpersuasive since claims 14 and 15 are directed to a method of using the polynucleotide encoding a diabetes-mediating protein whereas the claims of Group II are directed to use of the protein. These method claims are different/distinct from each other in methodologies, starting material, objectives, technical considerations, ingredients, end point or/and outcome. Furthermore, claim 15 is drawn to transgenic mammal expressing the protein thereof, wherein transgenic animal is biologically distinct from the cells set forth in claim 1). Thus, claims 1-11, 12-15, 19 and 22-23 stated above lack the same or corresponding special technical feature. The requirement is still deemed proper and is therefore made FINAL.

Since applicants elect SEQ ID NO:4 (i.e., human galectin-3), which reads on claims 8 and 23, for examination of the current application, and since claim 9 is directed to non-elected polypeptide sequences (see the recitation "...protein shown in FIGs. 6-48"), claim 9 is withdrawn from further consideration.

During a telephone conversation with Timothy Shea on 15 May 2003, applicants additionally elect SEQ ID NO:4 (human galectin-3) for examination. Affirmation of this election must be made by applicants in replying to this Office action. Claims 1-5, 9, 12-18, 20-21 and 24-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Therefore, elected claims 6-8, 10-11, 19 and 22-23 are under examination to the extent that they are drawn to the elected invention.

Objection to Specification/Claims

The disclosure is objected to because of the following informalities:

(1) In page 1, line 31 and page 2, line 1, "the presence and absence of" should be changed to "the presence or absence of".

(2) In page 2, line 9, "IEF" and "NEPHGE" should be spelled out for the first instance of use. See also page 4, line 31, "CMV" and MHC"; page 5, line 29, "ELISA" and RIA"; page 12, line 11, "2DGE"; page 26, line 22, "DEAE";

(3) In page 28, line 36, "diabetes mediating" should be changed to "diabetes-mediating".

(4) Claim 6 should be rewritten as an independent claim or a claim of appropriate claim dependency within the elected invention.

(5) Claim 8 is objected to as the proteins listed in the claim are referred from the specification. Note that the proteins listed in Tables 1 and 2 can be recited in claim per se

without referring to the tables, and that claims should stand on their own and not refer to the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 6-8 and 10-11 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 6-8 and 10-11 as written, do not distinguish the claimed peptides or polypeptides from naturally existing products. Claim 6 is directed to a product, even where, as here, it is written in product by process formate. The process steps do not per se present indicia of an alteration in the protein as compared to that protein as it naturally occurs. Thus, the method steps recited are accorded no weight.

The claims do not particularly point out any differences indicating the hand of man. In the absence of the hand of man, the claimed products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of man,.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-11, 19 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of the isolated galetin-3 polypeptide of SEQ ID NO:4 and a process of identifying a relation of the galectin-3 to diabetes state via analyzing test sample using an electrophoresis (see example 3, pages 48-49). Applicant is not in possession of using the galectin-3 for preventing or/and treating the diabetes.

The instant application sets forth that galectin-3 has protective activity (see the third paragraph, page 17). The specification, however, does not provide guidance and working examples or representative example as to how to use this "protective" protein to prevent against or treat diabetes disorder. The application disclosure does not reasonably establish an actual reduction to practice. Description of invention's reduction to practice, unaccompanied by any meaningful, distinguishing characteristics of the peptide variants stated above is insufficient to satisfy written description requirement of 35 U.S.C. §112, since inventors could have provided description of the variants or representative thereof of SEQ ID NO:4 polypeptide, since actual reduction to practice may demonstrate possession of embodiment of invention, but it does not necessarily describe what invention is, and since, in context of present case, disclosure of manner in which invention was reduced to practice does not satisfy more fundamental written description requirement set forth in Section 112.

Also, at issue is whether or not the claimed method would function for 'preventing diabetes..." recited in claim 19 of the instant application. The nature of the invention is such that it would require the administration of a diabetes-associated polypeptide to delaying the onset of diabetes or/and ameliorating the symptoms of diabetes in a subject at risk for development of diabetes. Nowhere in the specification, however, has prevention of diabetes by administering the galectin-3 protein and clinical effect thereof been described in a test animal. Rather, contrary to claim 10 that sets forth that the diabetes-mediating protein (e.g., galectin-3) has a positive effect on diabetes (i.e., reducing diabetes symptoms), claim 11 sets forth the same protein has a negative effect on diabetes (i.e., enhancing the development of diabetes). The specification does provide guidance and working examples as to the positive effect of the galectin-3 nor as to the negative effect of galectin-3. Thus, use of galectin-3 protein for treating or preventing diabetes is highly unpredictable.

Pugliese G. et al. (*Diabetes* (2000) 49(7), 1249-57) teach that galectin-3 has high affinity for advanced glycation end products (AGEs) which participate in non-enzymatic glycation associated pathogenesis of the dysregulated tissue remodeling that characterizes diabetic glomerulopathy, and that diabetic milieu induces or up regulates galectin-3 protein production (see abstract). Pugliese et al. also teach increased expression of galectin-3 involves in the pathogenesis of glomerulopathy (see the left column, page 1256), suggesting a negative role of galectin-3 in development of diabetes. Contrary to the "protective" role of gaclectin-3 as recited in claim 10, therefore, a method of treating or preventing comprising administering the galectin-3 protein is highly unpredictable. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. The

specification does not teach how to effectively prophylaxis of diabetes disorder or treatment thereof. The specification does not teach how to extrapolate data obtained from identification of association of galectin-3 with diabetes disorder to the development of effective in vivo mammalian including human therapeutic prevention or treatment, commensurate in scope with the claimed invention. Therefore, it is unclear that the skilled artisan could predict the efficacy of the modified blood exemplified in the specification.

In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the galectin-3 protein for preventing or treating diabetes, and absence of working examples providing evidence as to *in vivo* use of the protein, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed method of treating or preventing diabetes comprising administering galectin-3 protein with a reasonable expectation of success.

Applicant has disclosed only the galectin-3 polypetide of SEQ ID NO:4 and identified its association with diabetes; therefore, the skilled artisan cannot envision the contemplated use of galectin-3 in preventing or treating diabetes recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the clinically functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993).

One of skill in the art would reasonably conclude that the disclosure fails to provide written description regarding use of galectin-3 for preventing or treating diabetes disorder. Thus,

Applicant was not in possession of make and use of the claimed composition. *See University of California v. Eli Lilly and co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

In consideration of the issued stated *supra*, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 6-7, 10-11, 19 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite as to how and what in the claimed protein is mediated by the process of identification.

Claim 7 is not apparent regarding in which subject "altered expression" of the disclosed protein occurs. The dependent claims are also rejected.

Claim 10 recites "a protective protein"; the recitation is unclear regarding against what object and for what subject the protein protects. Also, claim 10 is indefinite as to the recitation "is capable of" protecting against the development of diabetes since 'is capable of" does not equate to indication that the claimed protein actually protect against the development of diabetes in a subject, for example. See also claims 11 and 19.

Claim 19 is indefinite in the recitation "diabetes-related disorder" because the recitation is not defined in the specification. Does the diabetes-relate disorder differ from or identical to the diabetes-related diseases as defined in page 10 of the specification ? The dependent claims are also rejected.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 6-7 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Ferre T. et al. (*Proc. Natl. Acad. Sci.* (1996) 93, 7225-7230).

Ferre et al. teach diabetes-associated protein, glucokinase (GK), which expression is altered during diabetes (see page 7225, the second paragraph of the right column, and abstract), i.e., very low level of GK expression. The Ferre et al. teaching meets the limitation of claims 6 and 7 of the current application.

Also, Ferre et al. teach that regulation of GK protein expression during diabetes is a useful approach to reducing diabetic hyperglycemia (see page 7229 the last paragraph), as applied to claim 10 of the instant application.

Claims 6-7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Jaffa, A. A. et al. (*Kid. Internat.* (1992) 41, 789-795).

Jaffa et al. teach a diabetes-associated protein, kallikrein, which expression level is reduced in streptozotocin induced diabetic animal (see abstract, and Figure 1), which meets the limitation set forth in claims 6 and 7 of the instant application.

Since Jaffa et al. also teach the changes in kallikrein activity contributes to the contrasting renal hemodynamic abnormalities in diabetic hyperglycemia (see the left column, page 794), the Jaffa et al. teaching anticipates claim 10 of the instant application.

Claims 6-7, 11, 19 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Eng, J. (US Pat. No. 5424286).

Eng teaches that expression of insulin, a diabetic polypeptide, is altered in non-insulin dependent diabetes mellitus (NIDDM) that is marked by hyperglycemia which can be treated by

administering insulin (see column 1, lines 28-39). The Eng teaching meets the limitations set forth in claims 6-7, 11, 19 and 22 of the instant application.

Claims 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Richardson, J. M. et al. (*J. Biol. Chem.* (1993) 266, 12690-12694).

Richardson et al. teach that GLUT 4 glucose transporter protein is a diabetes-associated factor as evidenced by its reduced expression in response to the diabetes disorder state (i.e., streptozotocin-induced insulin-deficient diabetes) (see abstract and Figure 5), which meets the limitation set forth in claims 6 and 7 of the instant application.

Claims 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by McLean M. P. et al. (*Endocrinology* (1995) 136, 3360-3368).

McLean et al. teach sterol carrier protein-2 (SCP2) which is characterized as a diabetes-associated protein factor as evidenced by a remarked increase of its expression level (3.5 fold) after diabetes induction (see abstract, Figures 5 and 6, and page 3366 which states that SCP2 is elevated in hepatic tissue of the diabetic animal despite the significantly lower level of SCP2 protein expresses in this tissue), which meets the limitation set forth in claims 6 and 7 of the instant application.

Claims 6-7, 10-11, 19 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Ellas, D. et al. (*Proc. Natl. Acad. Sci.* (1990) 87, 1576-1580).

Ellas et al. teach a diabetes-associated protein, i.e., heat shock protein 65 cross-reactive (hsp65-CR) antigen polypeptide, which expression level is elevated upon onset of diabetes (se Figure 1), which meets the limitation of claims 6-7 of the current application. Since administering hsp65-CR can induce or prevent diabetes (see the left column, page 1578), Ellas et al. teaching is applied to claims 10 and 11 of the instant application.

Also, Ellas et al. teach a method of treating diabetes comprising administering to a subject (mouse) suffering diabetes disorder (see page 1578, and Table 3 data), which meets the limitation set forth in claims 19 and 22 of the instant application.

Claims 6-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Brocia, R. W. et al. (US Pat. No. 5770355).

Brocia et al. teach a diabetes-associated protein, cholesteryl ester transfer protein (CETP), which expression level is increased during diabetes (see column 8, lines 35-40), which meets the limitation of claims 6-7 of the current application.

Claims 6-7, 11 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Girten, B. E. et al. (US Pat. No. 576001).

Girten et al. teach a diabetes-associated protein, cytokine IL-1, which expression level is altered during diabetes (se column 1, lines 44-49), which meets the limitation of claims 6-7 of the current application. Since the cytokine is a mediator of diabetes disease state (see column 9, lines 41-44) as evidenced by the fact that IL-1 cytokine induces islet nitro oxide which impair

islet function, decrease glucose-induced insulin release, i.e., the cytokine enhances the risk of a subject developing diabetes (see column 9, lines 42-5), which meets the limitation set forth in claim 11 of the instant application.

Also, Girten et al. teach a method of treating disease state, e.g., diabetes, comprising administering a compound, which is cytokine restraining peptide (see the patent claims 1-4), as applied to claim 19 f the instant application.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703-308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-y9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

SWL

Samuel Wei Liu, Ph.D.

May 27, 2003

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